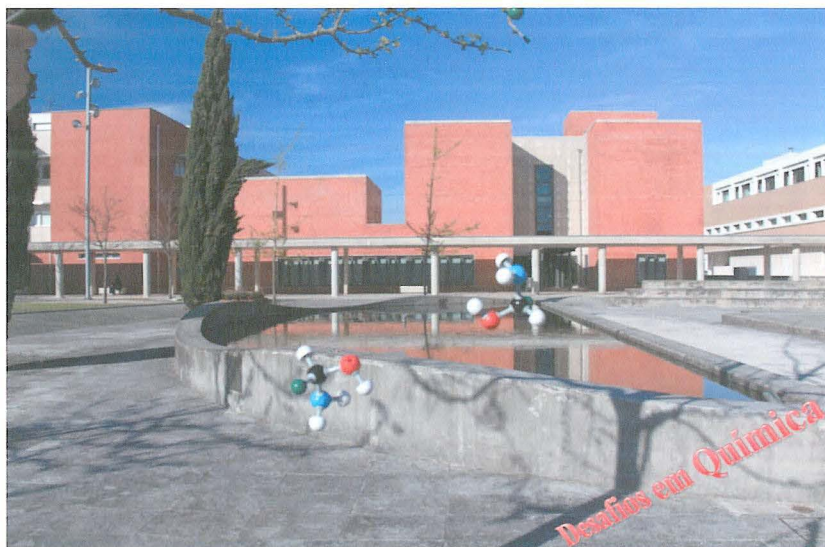


XXIII Encontro Nacional da SPQ



Aveiro 12 a 14 de Junho de 2013



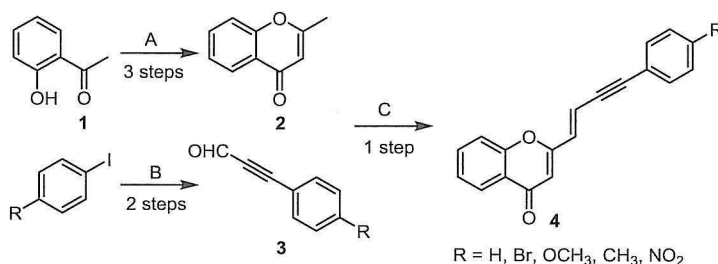
Synthesis of (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones

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Chromones are a well-known class of naturally occurring oxygen-containing heterocyclic compounds; many of them playing important biological functions in nature.^[1] Although 2-methylchromones are one of the scarcest classes of natural chromones, their synthesis and reactivity is well studied. They can participate in several chemical transformations such as oxidation, thiation, hydrogenation, photolysis, cycloaddition and condensation reactions, being useful targets in the synthesis of novel heterocyclic compounds.^[2] The acidity of the 2-methyl group, due to the low electron density at C-2 caused by oxygen atom and the α,β -unsaturated ketone system, led us to explore the condensation of 2-methylchromone **2**^[3] with propargyl aldehydes **3**^[4] in order to obtain new (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones **4** (Scheme 1). The starting material, 2-methyl-chromone **2** was prepared in a three step sequence starting from 2'-hydroxyacetophenone **1** while the propargyl aldehydes **3** were obtained from the reaction of the appropriate iodobenzene with propargyl alcohol and subsequent oxidation.

In this communication we will present the synthetic details of all described transformations as well as the structural characterization (by 1D and 2D NMR studies) of the new synthesized compounds.



Scheme 1

Acknowledgments: Thanks are due to the University of Aveiro, Fundação para a Ciência e Tecnologia (FCT, Portugal), European Union, QREN, FEDER and COMPETE for funding the QOPNA Research Unit (project PEst-C/QUI/UI0062/2011) and the Portuguese National NMR Network. Hélio Albuquerque also thanks FCT for his fellowship (SFRH/BI/51556/2011).

References

- [1] Sharma, S.K.; Kumar, S.; Chand, K.; Kathuria, A.; Gupta, A.; Jain, R. *Curr. Med. Chem.* **2011**, *18*, 3825.
- [2] Ibrahim, M. A.; Ali, T. E.; Alnamer, Y. A.; Gabr, Y. A. *Arkivoc* **2010**, (i), 98.
- [3] Hirao, I.; Yamaguchi, M.; Hamada, M. *Synthesis* **1984**, 1076.
- [4] a) Tretyakov, E. V.; Tkachev, A. V.; Rybalova, T. V.; Gatilov, Y. V.; Knight, D. W.; Vasilevsky, S. F.; *Tetrahedron* **2000**, *56*, 10075. b) Wadsworth, D. H.; Geer, S. M.; Detty, M. R. *J. Org. Chem.* **1987**, *52*, 3662. c) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Synthesis* **1984**, 728.



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Introduction

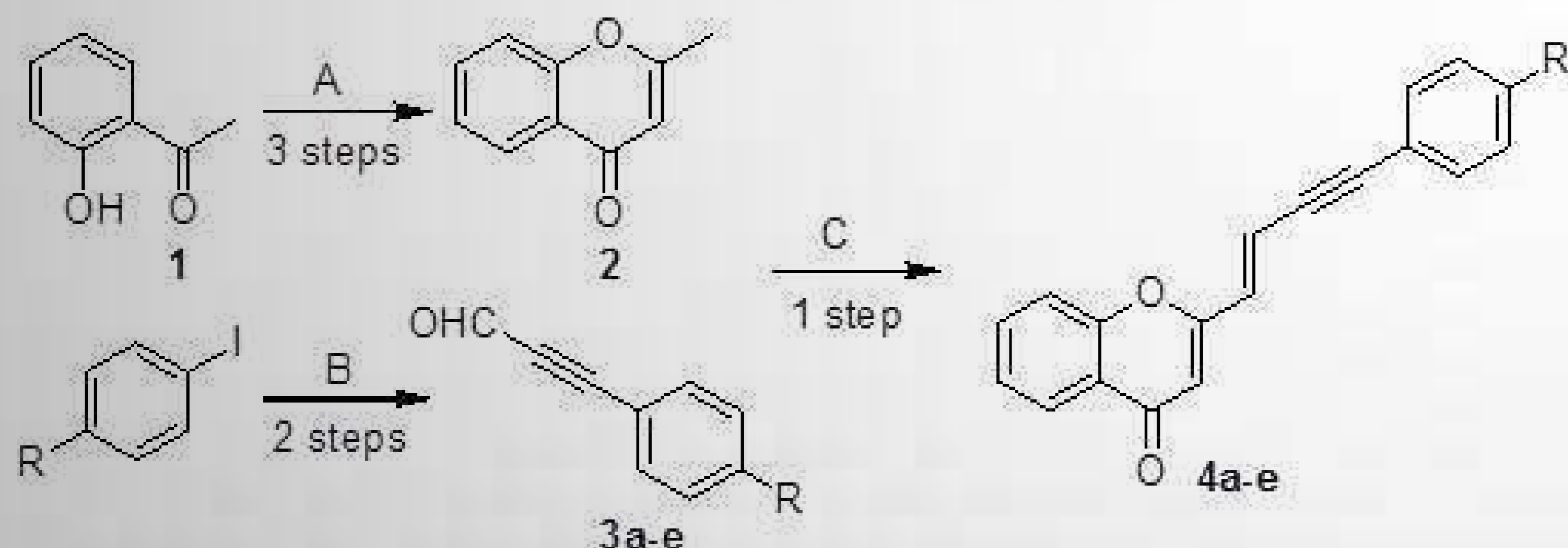
Chromones are a well-known class of naturally occurring oxygen-containing heterocyclic compounds; many of them playing important biological functions in nature [1]. Although 2-methylchromones are one of the scarcest classes of natural chromones, their synthesis and reactivity is well studied. They can participate in several chemical transformations such as oxidation, thiation, hydrogenation, photolysis, cycloaddition and condensation reactions, being useful targets in the synthesis of novel heterocyclic compounds [2]. The acidity of the 2-methyl group, due to the low electron density at C-2 caused by oxygen atom and the α,β -unsaturated ketone system, led us to explore the condensation of 2-methylchromones [3] with propargyl aldehydes [4].

Experimental section and results

The synthetic strategy for the preparation of (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones involved:

- The synthesis of 2-methylchromone **2** by a three step sequence starting from 2'-hydroxyacetophenone **1**.
- The synthesis of propargyl aldehydes **3** reacting the appropriated iodobenzene with propargyl alcohol and subsequent oxidation.
- The condensation of 2-methylchromone **2** with propargyl aldehydes **3a-e** leading to the desired (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones **4a-e**.

General procedure



Reaction Conditions:

A: (i) MeCOCl, dry pyridine, r.t., 12 h; (ii) NaH, dry THF, reflux, 2 h; (iii) *p*-TSA, DMSO, 100°C, 2 h.

B: (i) Pd(PPh₃)Cl₂, PPy, CuI, propargyl alcohol, toluene, 60 °C, 2h; (ii) activated MnO₂, ethyl acetate, reflux, 2h.

C: Sodium, dry EtOH, r.t., 4 h.

Results

Compound	R	Yield (%)
4a	H	52
4b	CH ₃	80
4c	OCH ₃	80
4d	Br	59
4e	NO ₂	30

[1] Sharma S. K., Kumar S., Chand K., Kathuria A., Gupta A., Jain R. *Curr. Med. Chem.* **2011**, *18*, 3825.

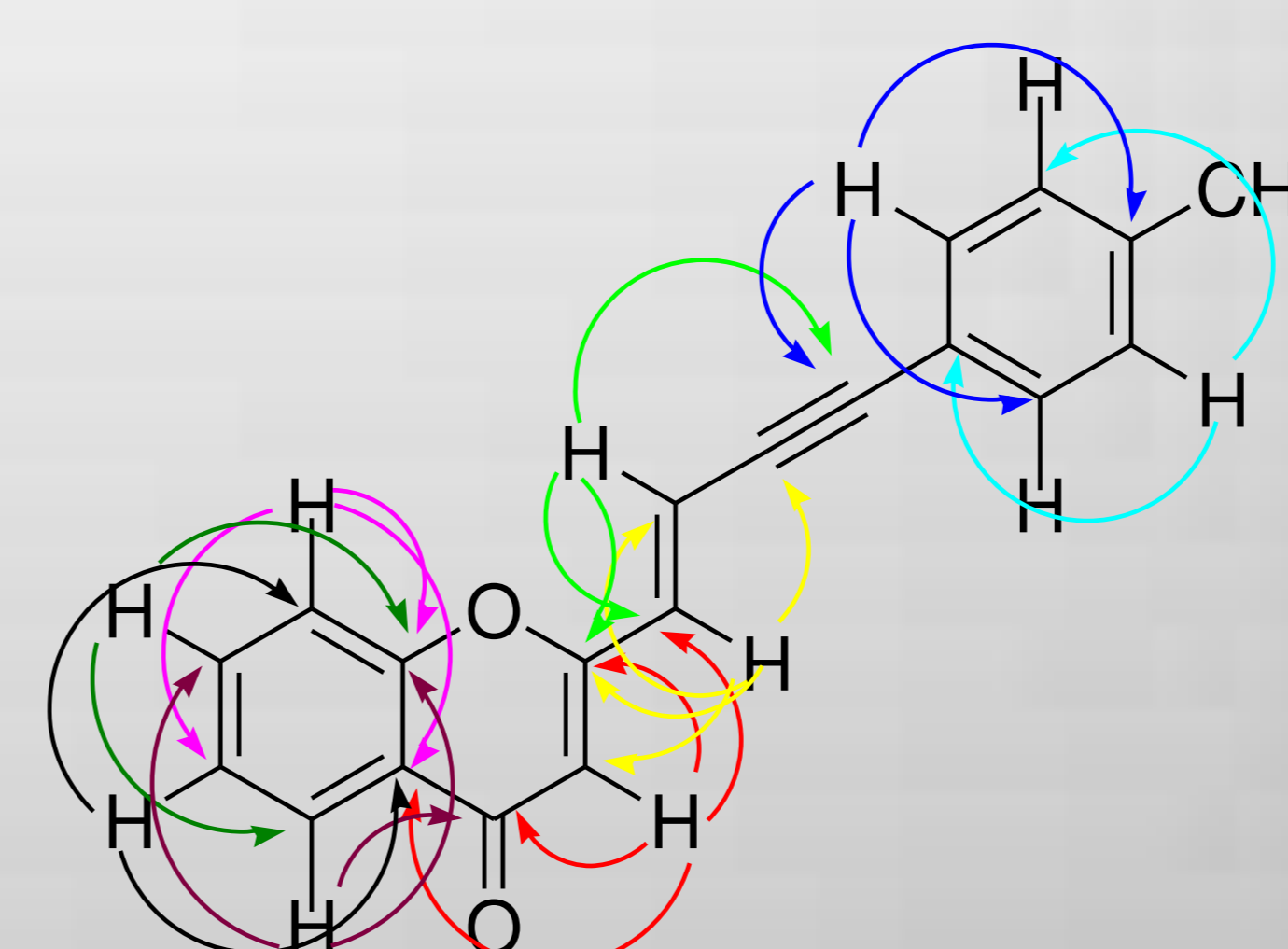
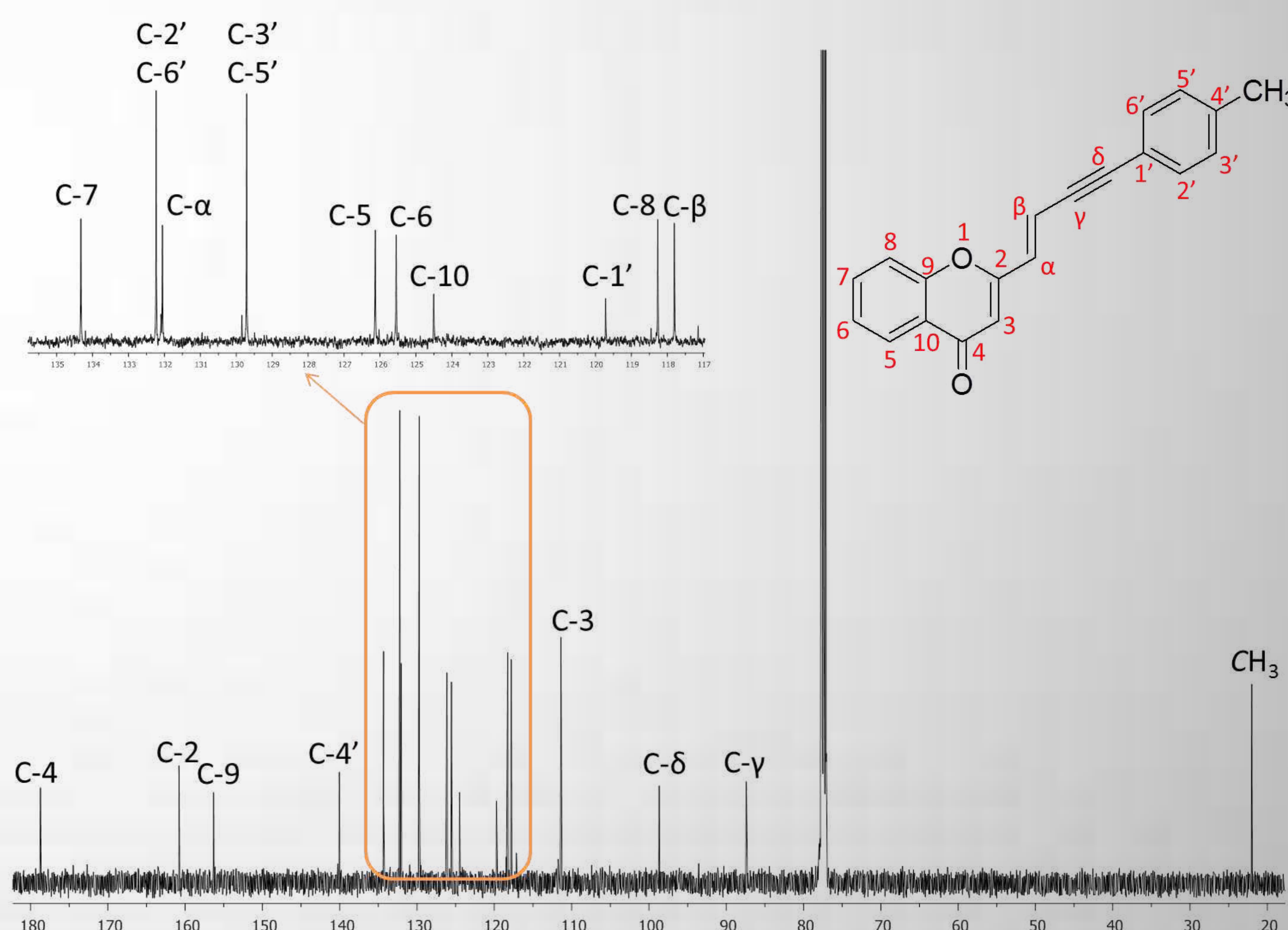
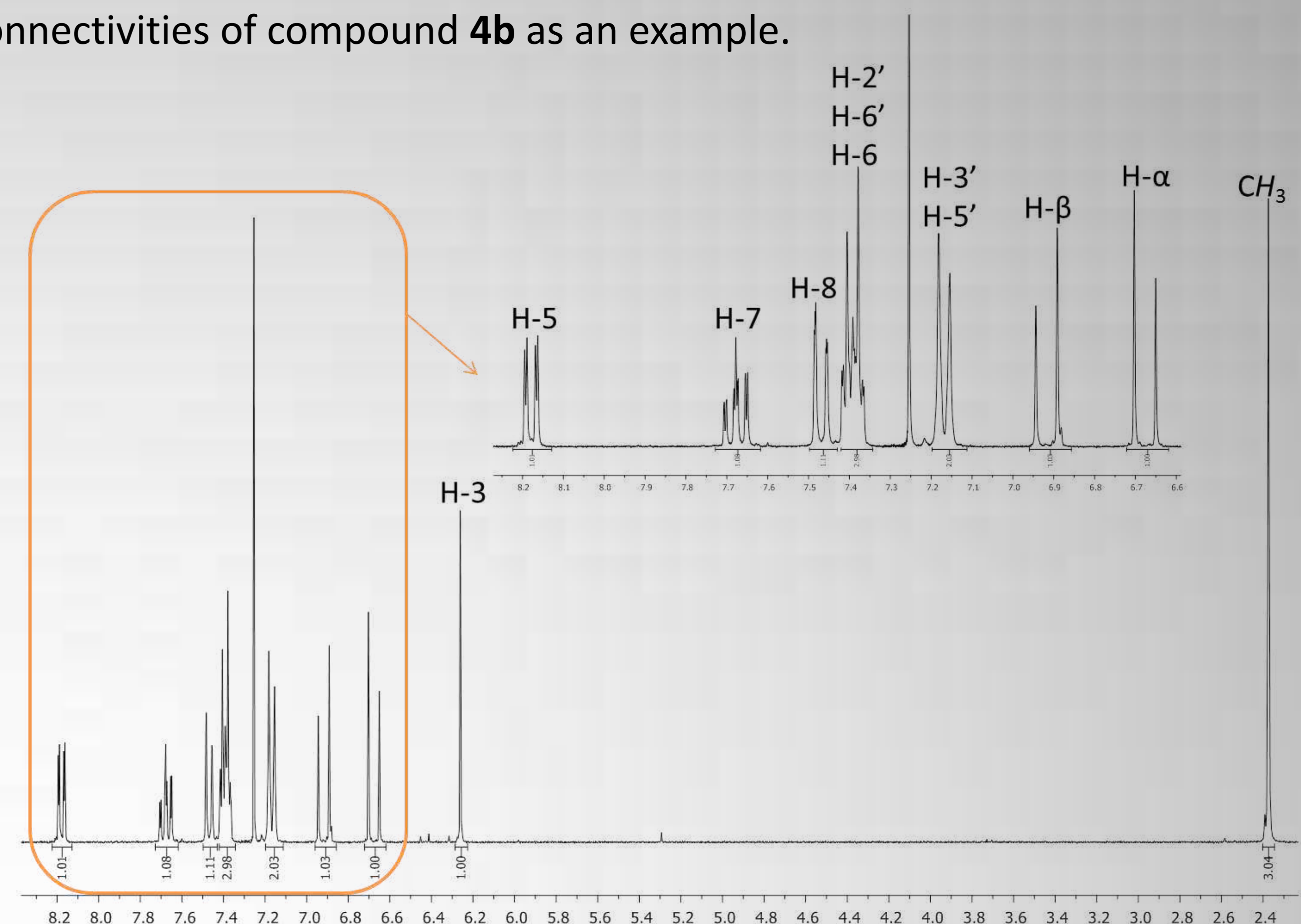
[2] Ibrahim, M. A.; Ali, T. E.; Alnamer, Y. A.; Gabr, Y. A. *Arkivoc* **2010**, (i), 98.

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Structural elucidation

The structural characterization of compounds **4a-e** was obtained by 1D and 2D-NMR studies. We present below the ¹H-NMR, ¹³C-NMR and HMBC connectivities of compound **4b** as an example.



Most important HMBC connectivities of compound **4b**.

Conclusions

The (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones **4a-d** were synthesized *via* aldol condensation of 2-methylchromone **2** (obtained *via* Baker-Venkataraman methodology) with propargyl aldehydes **3a-d** in moderate to good yields. Compound **4e** was obtained in low yield due to the degradation of the corresponding propargyl aldehyde during the condensation reaction.

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